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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 10/808,682 | 03/25/2004 | Charbel Haber | 21192 | 6196 |
| 210 | 7590 | 12/15/2006 | EXAMINER | |
| MERCK AND CO., INC P O BOX 2000 RAHWAY, NJ 07065-0907 | | | FORD, ALLISON M | |
| | | | ART UNIT | PAPER NUMBER |
| | | | 1651 | |

DATE MAILED: 12/15/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

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|------------------------------|--------------------------------------|-------------------------------------|--|
| Office Action Summary | Application No. 10/808,682 | Applicant(s) HABER ET AL. | |
| | Examiner Allison M. Ford | Art Unit 1651 | |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 21 September 2006.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-16 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-16 is/are rejected.
- 7) ☒ Claim(s) 12 and 13 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 25 March 2004 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Election/Restrictions

In the response received 21 September 2006 applicants responded to the election of species requirement in full, by electing the species of “diploid fibroblast cells” as the species of cell, and “viruses” as the species of cell product. Applicants traverse the election, stating that restriction is not proper because the inventions are not independent or distinct, as defined by the MPEP at 802.01; and that examination of all species would not present an undue burden on the Examiner, as all species are related.

In view of search results, the election of species requirement have been lifted, all species have been examined.

Claim Objections

Claim 12 is objected to because of a minor informality: the claim should begin with a definite article, it would be remedial to restate, “The method according to claim 10...”

Claim 13 is objected to because of a minor informality: line 1 should read, “...contained within cells that do not have a...”

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 13 and 14 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Applicants' claim 13 is directed to a method of harvesting a cell product contained within cells that do not have a cell wall, said method comprising: (i) culturing said cells in a culture medium under

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conditions appropriate for production of the desired cell product; (ii) suspending the cells in a suspension fluid; (iii) passing the suspended cells through a nozzle at a low pressure, wherein the outflow of the nozzle does not impinge on the outflow of a second nozzle or any other impingement surface, so that the cells are disrupted at a pressure of from about 5 to 100 psi and the cell product is released; and (iv) recovering the released cell product.

Claim 13 is considered indefinite because it is not clear if the pressure at which the cells are disrupted is intended to define the "low pressure" at which the cells are passed through the nozzle; it appears the pressures are one and the same measure. As such, claim 13 is further considered indefinite because it recites a broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation. Specifically, the claim requires the suspended cells to be passed through a nozzle at a "low pressure" (broad limitation), then also recites "the cells are disrupted at a pressure of from about 5 to 100 psi" (narrow limitation). Such claim language is considered indefinite since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. See MPEP § 2173.05(c).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 2, 8 and 10-16 are rejected under 35 U.S.C. 102(b) as being anticipated by Seifert et al (US Patent 5,721,120).

Applicants' claim 1 is directed to a method for disrupting cultured cells that lack a cell wall comprising passing the cells, suspended in a suspension fluid, through a nozzle at a low pressure, wherein

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the outflow of the nozzle does not impinge on the outflow of a second nozzle if multiple nozzles are present. Claim 2 requires the low pressure to range from 1 to 100 psi. Claim 8 requires the nozzle to have a tapered or conical shape. Claims 10-12 are directed to the type of cell, specifically animal cells, more specifically diploid fibroblast cells such as VERO, CHO, and MRC-5 diploid lung cells. Claims 13-16 are directed to methods of recovering a desired cell product, wherein the methods comprise first culturing cells in suitable conditions to induce intracellular production of the desired cell product, and then subjecting the cells to the method disclosed in claim 1. Claims 13-16 further describe the type of cell product as a polysaccharide, a protein, or a virus, specifically a Varicella virus.

Seifert et al claims a method for the disruption of cultured cells which lack a cell wall, comprising passing cells suspended in a culture fluid through a low pressure impinging jet device at a pressure of from about 5 to 100 psi (Seifert et al, claims 1 and 4); though applicants do not specifically require the 'nozzle' to be part of an impinging jet device, said device does include a nozzle. Seifert et al further claim a method for disrupting cells to harvest a cell product, comprising culturing cells in a culture medium under culture conditions suited to bring about the production of the desired cell product; suspending the cells in a suspension fluid; passing the suspended cells through a low pressure impinging jet device so that the cells are disrupted at a pressure of from about 5 to 100 psi and the cell product is released; and recovering the released cell product (Seifert et al, claim 5). The cell product can be a protein, a virus, including a Varicella virus, or a polysaccharide (Seifert et al, claims 6-10 and col. 2, ln 61-66). The cells can be animal cells, including VERO cells, CHO cells, diploid fibroblast cells or MRC-5 diploid lung cells (Seifert et al, claims 2, 3, & 9).

In Fig. 1 of Seifert et al the impinging jet device is shown to have two tapered or conical nozzles, wherein the outflow of each stream impinges upon one another, creating the force. It is noted that applicants' claims have a proviso that if a second nozzle is present, the outflow of the [first] nozzle does not impinge on the outflow of a second nozzle; the claimed method of Seifert et al does not recite or

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require two nozzles as shown in Fig. 1, but rather recites use of a low pressure impingement device, which is being interpreted as a single jet. It is further noted that in Example 2 Seifert et al discloses multiple jets can be used in series (See Seifert et al, col. 4, ln 66); a "series" configuration is understood to mean to infer sequential arrangement, so that the streams do not impinge upon one another, but rather upon a surface in a series. However, the nozzle shape illustrated in Fig. 1 is relied upon to show that Seifert et al teaches a conical or tapered nozzle. Therefore the reference anticipates the claimed subject matter.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1-12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Seifert et al (US Patent 5,721,120).

Applicants' claim 1 is directed to a method for disrupting cultured cells that lack a cell wall comprising passing the cells, suspended in a suspension fluid, through a nozzle at a low pressure, wherein the outflow of the nozzle does not impinge on the outflow of a second nozzle if multiple nozzles are present. Claims 2-4 limit the range of the low pressure. Claims 5-9 are directed to the shape of the nozzle and to the size of the orifice in the nozzle. Claims 10-12 are directed to the type of cell, specifically animal cells, more specifically diploid fibroblast cells such as VERO, CHO, and MRC-5 diploid lung cells.

The teachings of Seifert et al are set forth above. Generally, Seifert et al disclose a method for the disruption of cultured cells which lack a cell wall, comprising passing cells suspended in a culture

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fluid through a low pressure impinging jet device at a pressure of from about 5 to 100 psi (Seifert et al, claims 1 and 4). The nozzle of Seifert et al can be conical or tapered (Seifert et al, Fig. 1).

Seifert et al does not disclose narrower pressure ranges, as are currently claimed by applicant; however Seifert et al does teach that the operational pressure is a result effective variable, the disclosed low operating pressure resulting in a gentle disruption which does not result in destruction of the desired cell products (See Seifert et al, col. 3, ln 40-52). Therefore, it would have been obvious to one of ordinary skill in the art, at the time the invention was made, to optimize the operating pressure of the impinging jet device used in the method of Seifert et al, within the claimed range of 5 to 100 psi, as a matter of routine experimentation. Moreover, at the time of the claimed invention, one of ordinary skill in the art would have been motivated by routine practice to optimize the operating pressure of the impinging jet device used in the method of Seifert et al, with a reasonable expectation for successfully disrupting cells and harvesting the cell products thereby produced. Generally, differences in concentration will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration or temperature is critical or produces unexpected results. Where the general conditions of a claim are disclosed by the prior art it is not inventive to discover the optimum or workable ranges by routine experimentation, See *In re Aller*, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955). Also note that where the claimed ranges overlap or lie inside ranges disclosed by the prior art a prima facie case of obviousness exists. See *In re Wertheim*, 541 F.2d 257, 191 USPQ 90 (CCPA 1976); *In re Woodruff*, 919 F.2d 1575, 16 USPQ2d 1934 (Fed. Cir. 1990).

Furthermore, Seifert et al does not disclose the exact dimensions of the orifice of the nozzle, nor does he suggest the nozzle has a tapered entrance as well as a tapered exit; however, modifications of shape and dimensions are considered to be prima facie obvious, as long as the device remains capable of operating at the claimed pressure of 5 to 100 psi. Specifically, with regards to the matter of the shape of the nozzle, the decision in *In re Dailey*, 357 F.2d 669, 149 USPQ 47 (CCPA 1966) is cited in support of

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the reasoning that the shape of an object is an optimizable matter of choice, absent persuasive evidence that use of a nozzle with the particular claimed configuration is significant. With regards to the size of the orifice in the nozzle, the decision in *In Gardner v. TEC Systems, Inc.*, 725 F.2d 1338, 220 USPQ 777 (Fed. Cir. 1984), cert. denied, 469 U.S. 830, 225 USPQ 232 (1984), is cited in support of the reasoning that, because the device used in the method of Seifert et al is able to perform the method as currently claimed (operate at the claimed psi), and may only differ in relative dimensions of a device used to perform the claimed method, differences in sizes or dimensions of parts of the apparatus used to perform the method are not sufficient to patentably distinguish the claimed method from the method disclosed in the prior art.

Therefore the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

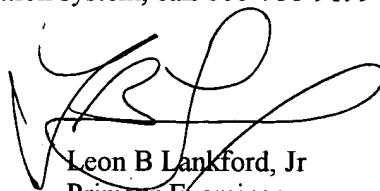
Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Allison M. Ford whose telephone number is 571-272-2936. The examiner can normally be reached on 7:30-5 M-Th, alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached on 571-272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.



Leon B Lankford, Jr
Primary Examiner
Art Unit 1651